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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,591	11/30/2001	Tamotsu Kondow	216583US0XCONT	3947

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,591	KONDOW ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 26-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,26 and 28-35* is/are rejected.

7)☒ Claim(s) *2,11,27 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8/04* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

CONTINUED EXAMINATION

1. Applicant's RCE and the amendment filed on August 26, 2004 have been entered. The claims pending in this application are claims 1-11 and 26-36.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 3, 4, 7, 8, 19, 26, 28, 29, 32, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Dower *et al.*, (US Patent No. 5,547,839).

Regarding claim 1, Dower *et al.*, teach a method for determining a nucleotide sequence of a single nucleic acid molecule, which comprises: (a) immobilizing a nucleic acid molecule onto the surface of a solid; (b) annealing a primer to said nucleic acid molecule, wherein said primer has a sequence complementary to a part of a sequence of the nucleic acid molecule; (c) providing a solution which contains a DNA polymerase and only one type of dye-labeled dNTP, where N is A, T or U, G or C, or an RNA polymerase and only one type of dye-labeled NTP, where N is A, U, G or C, to said immobilized nucleic acid molecule, and allowing the dye-labeled dNTP or NTP to react with the 3' end of said primer, whereby the dye-labeled dNTP or NTP, which forms a base-pair with a base in the nucleic acid molecule at a position where the dye-labeled dNTP or NTP reacts with the 3' end of said primer and; is bound to the primer by

action of the polymerase; (d) detecting a bound, dye-labeled dNTP or NTP; (e) disrupting the dye molecule of the bound, dye-labeled dNTP or NTP; (e) repeating (c) to (e) while changing the type of dye-labeled dNTP or NTP in turn, to sequentially bind dNTPs or NTPs which forms a base-pair with the nucleotides of the nucleic acid molecule; and (g) determining a nucleotide sequence of the nucleic acid molecule based on the types of the sequentially bound dNTPs or NTPs (see columns 23-26 and claims 1-7 in columns 28-30).

Regarding claim 26, Dower *et al.,* teach a method for determining a nucleotide sequence of a single nucleic acid molecule, which comprises: (a) immobilizing a primer onto the surface of a solid, wherein the primer comprises a sequence complementary to a part of a sequence in the nucleic acid molecule; (b) annealing a nucleic acid molecule to the immobilized primer; (c) providing a solution which contains a DNA polymerase and only one type of dye-labeled dNTP, where N is A, T or U, G or C, or an RNA polymerase and only one type of dye-labeled NTP, where N is A, U, G or C, to said immobilized nucleic acid molecule, and allowing the dye-labeled dNTP or NTP to react with the 3' end of said primer, whereby the dye-labeled dNTP or NTP, which forms a base-pair with a base in the nucleic acid molecule at a position where the dye-labeled dNTP or NTP reacts with the 3' end of said primer and; is bound to the primer by action of the polymerase; (d) detecting a bound, dye-labeled dNTP or NTP; (e) disrupting the dye molecule of the bound, dye-labeled dNTP or NTP; (e) repeating (c) to (e) while changing the type of dye-labeled dNTP or NTP in turn, to sequentially bind dNTPs or NTPs which forms a base-pair with the nucleotides of the nucleic acid molecule; and (g) determining a nucleotide sequence of the nucleic acid molecule based on the types of the sequentially bound dNTPs or NTPs (see columns 23-26 and claims 1-7 in columns 28-30).

Regarding claims 3 and 28, Dower *et al.*, teach optically detecting the dye molecule of said dye-labeled dNTP or NTP (see columns 25 and 26).

Regarding claims 4 and 29, Dower *et al.*, teach exciting dye molecules by irradiation of a laser beam and detecting a fluorescent signal (see column 20, lines 61-67, column 21, lines 1-9 and columns 25 and 26).

Regarding claims 7, 8, 32, and 33, Dower *et al.*, teach that said dye is a fluorescent dye. wherein said dye-labeled dNTP is labeled with rhodamine, tetramethyl rhodamine (fluorescein) Rhodamine 6G, fluorescein isothiocyanate, or 4-fluoro-7-nitro-berlzofurazon (Texas Red) (see column 21, last paragraph and column 26, lines 27-67).

Regarding claims 10 and 35, Dower *et al.*, teach that said dNTP or NTP is each labeled with the same dye (see column 25, lines 65-67).

Therefore, Dower *et al.*, teach all limitations recited in claims 1, 3, 4, 7, 8, 10, 26, 28, 29, 32, 33, and 35.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 5 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower *et al.*, (1996) as applied to claims 1, 3, 4, 7, 8, 10, 26, 28, 29, 32, 33, and 35 above, and further in view of Mathies *et al.*, (US Patent No.5,091,652, published on February 25, 1992).

The teachings of Dower *et al.*, have been summarized previously, *supra.*

Dower *et al.*, do not disclose to detect fluorescence signals using a confocal fluorescence microscope system as recited in claims 5 and 30. However, in their method, fluorescence signal was detected using a microscope system (see column 13, lines 43-62).

Mathies *et al.*, teach to detect fluorescence signals using a confocal fluorescence microscope system (i.e., a laser excited confocal microscope fluorescence scanner) (see abstract and Figure 1).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the detection recited in claim 1 using a confocal fluorescence microscope system in view of the patents of Dower *et al.*, and Mathies *et al.*. One having ordinary skill in the art would have been motivated to do so because Mathies *et al..*, have successfully used a confocal fluorescence microscope system to detect fluorescence signals and the simple replacement of one well known fluorescence detection device (i.e., a microscope system taught by Dower *et al.*,) from another well known fluorescence detection device (i.e., a confocal fluorescence microscope system taught by Mathies *et al..*,) during the

process of detecting fluorescence signals would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the experimental results.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

6. Claims 6 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower *et al.*, (1996) as applied to claims 1, 3, 4, 7, 8, 10, 26, 28, 29, 32, 33, and 35 above, and further in view of Anazawa *et al.*, (US Patent No.6,242,193, priority date: July 30, 1999).

The teachings of Dower *et al.*, have been summarized previously, *supra.*

Dower *et al.*, do not disclose that said disrupting the dye molecules in (e) comprises irradiating with a laser beam stronger than the laser beam in (d) as recited in claims 6 and 31. However, Dower *et al.*, teach disrupting the dye molecules using enzymatic, chemical and other possible methods (see column 21, lines 29-42).

Anazawa *et al.*, teach detecting and disrupting the dye molecules using a laser beam (see abstract). Since the intensity of laser used for disrupting the dye molecules must stranger than

the intensity of laser used for detecting the dye molecules, Anazawa *et al.*, disclose claims 6 and 31.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 6 and 31 wherein said disrupting the dye molecules in (e) comprises irradiating with a laser beam stronger than the laser beam in (d) in view of the patents of Dower *et al.*, and Anazawa *et al.*. One having ordinary skill in the art would have been motivated to do so because Anazawa *et al..*, have successfully used a laser beam for detecting and disrupting the dye molecules and the simple replacement of one well known fluorescence disrupting method (i.e., the disrupting method aught by Dower *et al.*,) from another well known fluorescence disrupting method (i.e., the disrupting method taught by Anazawa *et al..*, using a laser beam) during the process of performing the method recited in claims 6 and 31, would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the experimental results.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

7. Claims 9 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower *et al.*, (1996) as applied to claims 1, 3, 4, 7, 8, 10, 26, 28, 29, 32, 33, and 35 above, and further in view of Caldwell *et al.*, (US Patent No. 5,112,736, published on May 12, 1992).

The teachings of Dower *et al.*, have been summarized previously, *supra.*

Dower *et al.*, do not disclose that said dye-labeled NTP is labeled with rhodamine, tetramethyl rhodamine (iuorescein), Rhodamine 6G, fluorescein isothiocyanate, or 4-iuoro-7-niko-benzofurazon (Texas Red) as recited in claims 9 and 34.

Caldwell *et al.*, suggest that a DNA sequencing method can be used for sequencing a RNA fragment (see column 17, lines 10-37).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 9 and 34 wherein said dye-labeled NTP is labeled with rhodamine, tetramethyl rhodamine (iuorescein), Rhodamine 6G, fluorescein isothiocyanate, or 4-iuoro-7-niko-benzofurazon (Texas Red) in view of the patents of Dower *et al.*, and Caldwell *et al.*. One having ordinary skill in the art would have been motivated to do so because Caldwell *et al.*., suggest that a DNA sequencing method can be used for sequencing a RNA fragment (see column 17, lines 10-37) and fluorescent-labeled NTPs are commercially available. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make use the DNA sequencing method taught by Dower *et al.*, for sequencing a RNA fragment.

Conclusion

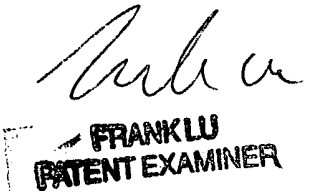
8. Claims 2, 11, 27, and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is 571-272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571) 272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.



Frank Lu
PSA
December 13, 2004